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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/330,262 | 06/11/1999 | JOHAN THEVELEIN | 6-1032-041 | 9212 |

803 7590 09/10/2003

STURM & FIX LLP
206 SIXTH AVENUE
SUITE 1213
DES MOINES, IA 50309-4076

EXAMINER

LAMBERTSON, DAVID A

| ART UNIT | PAPER NUMBER |
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1636

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DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/330,262

Applicant(s)

THEVELEIN ET AL.

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 9, 10, 12, 14-23, 26-35, 38 and 40-61 is/are pending in the application.

4a) Of the above claim(s) 26-35 is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9, 10, 12, 14-23, 38 and 40-61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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DETAILED ACTION

Receipt is acknowledged of a reply, filed June 20, 2003 as Paper No. 14, to the previous Office Action. Amendments were made to the claims. Specifically, applicant cancelled claim 36 and added new claims 60 and 61.

Claims 1-7, 9, 10, 12, 14-23, 26-35, 38 and 40-61 are pending in the instant application. Claims 26-35 are withdrawn as being drawn to a non-elected invention. Claims 1-7, 9, 10, 12, 14-23, 38 and 40-61 are under consideration in the instant application. Any rejection of record in the previous Office Action, mailed December 17, 2002 as Paper No. 12, that is not addressed in this action has been withdrawn.

Claim Objections

Claim 4 is objected to under 37 CFR 1.75(c) as being in improper form because it is multiply dependent on claims 1 and 3, but the multiple dependency is not recited in the alternative. It is noted that claim 3, from which claim 4 depends, is also dependent on claim 1 and therefore contains all of the recited limitations as set forth in claim 1; therefore, it would be remedial to simply remove the recitation of claim 1 from the body of claim 4.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 7, 9, 12, 1438, 40, 41 and 51-61 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Specifically, the claim is directed

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to yeast strains which can arise naturally, therefore there is an absence of the "hand of man" in the claimed invention. Indication that the claims are either "isolated" or "recombinant" would be sufficient to show the "hand of man" which is necessary to demonstrate that the claimed subject matter was invented. **This is a new rejection not necessitated by amendment.**

Claim Rejections - 35 USC § 112, First Paragraph

Claims 7, 9, 10, 12, 14, 38, 40, 41 and 51-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons set forth in the previous Office Action, Paper No. 12, and is now applied to newly added claim 60 and 61.**

Response to Arguments Concerning Claim Rejections - 35 USC § 112, First Paragraph

Applicant's arguments filed June 20, 2003 have been fully considered but they are not persuasive. Applicant's arguments consist of the following points:

1. That the *fil* phenotype has been identified by its survival rate and stability against freezing in pieces of dough, each of which can be evaluated without the need of a reference strain.
2. That the specification discloses "several mutation methods resulting into [sic] the *fil* strains and *fil* strains thus obtained," therefore the specification must necessarily describe the resulting strains.

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3. That two specific mutations disclosed in the specification, in the CYR1 gene and the GPR1 gene, represent the entire genus of *fil* mutations.
4. That example 7 of the instant specification describes a means for the construction of new *fil* strains.

Applicant's arguments are not convincing for the following reasons:

1. The fact that the *fil* phenotype can be *determined* for a given strain does not describe the strain itself. This is an enablement argument whereas the rejection was made on the basis of a lack of written description. As set forth in the previous Office Action, there is no description of a particular type of mutation (e.g., in a specific gene, or specific type of gene) that results in the production of the *fil* phenotype, and there is no structure-function relationship correlating a gene function (or lack thereof) to the *fil* phenotype. Furthermore, there are only two specific examples of genes which, when mutated, result in the *fil* phenotype; however, there is no structure-function correlation between even these particular mutations and the resulting *fil* phenotype that suggests a corresponding mutation in a different gene will result in the *fil* phenotype. A phenotype is merely the functional aspect of the yeast strain in question, where the function is provided by the structural make-up (i.e., the genome) of the yeast strain. The fact of the matter is the skilled artisan could not look at the genotype of a given yeast strain and determine that the strain had a *fil* phenotype based on the description provided by the instant specification. In other words, the skilled artisan could not envision the broad genus of yeast strains that have a *fil* phenotype because applicant has not provided a structure-function relationship between an affected gene and the desired phenotype. Therefore, a method of screening a yeast strain for the *fil* phenotype

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of is not sufficient to satisfy the written description requirement for the actual strains identified by the method, which are being claimed in the instant case.

2 and 4. The fact that there are general methods of making a *fil* strain doesn't indicate a structure-function relationship that would allow the skilled artisan to envision the entire genus of the claimed invention. Example 7 is simply one method of obtaining possible *fil* phenotypes, as well as many other types of phenotypes. Applicant is reminded that this is a written description rejection, and not an enablement rejection where the ability to make a strain is brought into question. Furthermore, the rejected claims are not drawn to a method of making a strain, but to the resulting strain. Thus, the fact that there exist very general mutagenesis methods by which to make a strain does not necessarily indicate that the entire genus of strains that is claimed to result from the methods has been described. In the instant case, the method for making the strains involves *random mutagenesis*, which by definition suggests that the procedure does not follow a specific and repeatable process. As a result, the strains produced can vary greatly with respect to one another, especially on the genomic level, which is the structural determinant for the functional phenotype. The fact of the matter is that the instant specification does not describe a linking structural/genomic feature for the resulting strains having the functional *fil* phenotype (e.g., a particular gene or set of genes that, when mutated, gives the desired phenotype; i.e., what is the genomic/structural component of the phenotypic/functional feature?), despite the fact that the specification teaches how to generate such a functional phenotype. Again, describing *how to make a strain* does not allow the skilled artisan to *envision the broad genus of strains* that are claimed in the instant invention. Thus, the instant specification does not describe the entire

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genus of strains claimed in the instant application simply by describing a method by which these strains can be made.

3. The two specific mutations as described in the instant specification are not considered to be a representative number of examples of mutations that result in the *fil* phenotype. The reason is because there is no structural or functional feature that is shared, even between these two genes, which would allow the skilled artisan to envision the mutations in a yeast gene that would yield a *fil* phenotype. Again, there is no structure-function relationship that is presented between these genes and the resulting *fil* phenotype, therefore the argument is not persuasive to show that applicant was in possession of the claimed genus.

In conclusion, applicant's arguments are not sufficient to overcome the written description rejection for the reasons discussed above. As a result, the rejection is maintained.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9, 10, 12, 14-23, 38 and 40-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection not necessitated by amendment.**

Claim 1 is rejected as being indefinite for the following reasons:

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(A) Starting with the 12th line, the claim recites the limitation wherein “those of the surviving cells which respond to the following criteria which characterize the *fil* phenotype are selected” and then recites a number of criteria in an improper Markush-type group.

First, it is unclear what is meant by “respond to the following criteria;” does this mean the surviving cells have the phenotypes as set forth in the subsequent criteria, or does it mean the cells do something unknown in response to the criteria. For instance, it is unclear if the surviving cells do something when exposed to a CO₂ release at least equal to 80% of the starting strain, or if the surviving cells are capable of a release of CO₂ at least equal to 80% of the starting strain.

Second, it is unclear if the “surviving cells” must “respond” to one of the criteria or all of the criteria as set forth in the body of the claim. This is further complicated in depending claims where only one particular member of the criteria is modified, i.e., claim 2, which refers to an ability to assimilate alcohol. As it regards claim 2, it is unclear if the strain must maintain all of the criteria set forth in claim 1 as well as the alcohol assimilation property set forth in claim 2, or merely one of the criteria set forth in claim 1 and the limitation set forth in claim 2.

Third, it is unclear what the criteria actually are in many of the bulleted groups. For example, the first bulleted group indicates “a growth, evaluated by production or production yield of biomass over sugar in a given time or by growth rate.” It is unclear if this means evaluated by production or by growth rate, or if it means production yield of biomass over sugar in a given time or by growth rate, or if it means only one of the parameters.

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Fourth, specifically in the first bulleted section of the claim, the limitation states “a growth, evaluated by production.” It is unclear what is being measured because it is unclear what is being produced.

Fifth, the term “repeated culture” is indefinite because it is unclear how many times the culture must be repeatedly grown in order to satisfy the limitation in the claim.

Finally, the term “perfectly stable” in claim 1 is a relative term which renders the claim indefinite. The term “perfectly stable” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(B) There is no positive process step recapitulating the method as recited in the preamble of the claim. Specifically, there is no ultimate step indicating that “a yeast strain conserving stress resistance in the presence of fermentable sugars” has been obtained. In the absence of such a step the method is incomplete because it has no endpoint. Without such an endpoint, the metes and bounds of the claim are not defined, and the claim is rendered indefinite. It would be remedial to indicate a step at the end of the claim stating: “thereby obtaining a yeast strain conserving stress resistance in the presence of fermentable sugars.”

Claim 4 is rejected as being indefinite because of the recitation of the step “the segregants issued from this industrial mutant are crossed with a laboratory haploid strain to select the segregant issued from this industrial mutant giving to the polyploids obtained with the laboratory strain an improvement in the required properties.” Additionally, the claim recites the limitation wherein “the segregants thus selected are crossed one with the other.” For the sake of clearly indicating the confusion with this step, the Examiner has broken the limitation into sections as

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follows: (a) the segregants issued from this industrial mutant are (b) crossed with a laboratory haploid strain to (c) select the segregant issued from this industrial mutant (d1) giving to the (d2) polyploids obtained (e) with the laboratory strain an improvement in the (f) required properties. First, there is no step in which segregants are isolated from an industrial strain, as indicated in part (a), therefore the starting material of the method is unclear. Second, it is unclear if “crossed” is meant to indicate a mating step between an industrial strain and a laboratory strain in part (b) because there is no indication that a diploid/polyploid is obtained. Third, it is unclear what is meant by step (c) all together: is a diploid being selected from the putative mating step; is it simply that a different segregant is now being selected from the original starting industrial mutant; is an individual spore being selected from the industrial/laboratory strain diploid that may have been selected in step (b)? Fourth, it is unclear what is (d1) giving something to a polyploid (d2) that has not even been obtained in the step, despite the fact that the limitation states that one has been obtained. This is terribly unclear. Fifth, again, it is unclear what is meant in part (e) where it is indicated that the polyploid is obtained with a laboratory strain: is the limitation supposed to indicate the polyploid that was putatively obtained by mating the industrial mutant with the laboratory strain; has a separate polyploid been obtained from the mating of laboratory strains alone? This also is terribly unclear. Sixth, the “required properties” that are being improved are unclear. This has no antecedent basis in the claim itself, or any of the claims from which it depends. Finally, the claim refers to segregants that have been selected, and crossing them with one another. Where have segregants been selected? What are these segregants: laboratory strains, industrial strains, polyploids, a spore from a polyploid, etc.?

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Again, there is no antecedent basis for these "selected segregants." The claim must be appropriately amended to clarify what method steps are actually being performed in the claim.

Claims 3, 4, 12, 51, 55-57 and 60-61 is rejected as being indefinite for the recitation of the term "industrial strain" because it is unclear what defines an "industrial strain" of yeast. Is an "industrial strain" one that is used in a laboratory setting in an industry/company? It is unclear what characteristics define an industrial yeast strain from a non-industrial yeast strain, therefore the limitation is indefinite.

Claims 15-23 are indefinite for failing to begin with an article. In order for the claim language to be in proper English vernacular, the claim should properly begin with an indefinite article. It would be remedial to amend the claims to begin with an article such as "A," "An," or "The."

Claims 5 and 48-50 recite the limitation "selected *fil* strains" in the preamble of the claim. There is insufficient antecedent basis for this limitation in the claim. There is no indication of a "selected *fil* strain" in any of the claims from which claims 5 and 48-50 depend.

Claims 2, 14 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This rejection is maintained for reasons set forth in the previous Office Action, Paper No. 12.**

The term "bad smell or a bad or abnormal taste" in claims 2, 14 and 57 is a relative term which renders the claim indefinite. The term " bad smell or a bad or abnormal taste " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite

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degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Response to Arguments Concerning Claim Rejections - 35 USC § 112, Second Paragraph

Applicant's arguments filed June 20, 2003 as Paper N. 14 have been fully considered but they are not persuasive. Applicant's arguments are as follows:

1. The rejection does not take into consideration the common knowledge of the skilled artisan.
2. That evaluation by a panel provides a solution to the definition of "bad smell or a bad or abnormal taste."

Applicant's arguments are not convincing for the following reasons:

1. The limitation "bad smell or a bad or abnormal taste" has nothing to do with common knowledge of the skilled artisan. The limitation "bad smell or a bad or abnormal taste" is predicated on opinion alone, as one person may find something tastes bad while another may find the same thing tastes good. As a result, applicant's rationale is not persuasive.
2. The evaluation by a panel cannot define something as tasting good or bad as it pertains to the instant invention. Applicant has essentially argued that the definition of the limitation "bad smell or a bad or abnormal taste" is conditional, and dependent on the opinion of others, which may change over time, or depending on the constituency of the panel. This is the definition of indefinite in that it has constantly changing boundaries.

In conclusion, applicant has not provided an acceptable rationale as to why the limitation "bad smell or a bad or abnormal taste" is definite in contrast to the rejection at hand. As a result, the rejection is maintained.

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Allowable Subject Matter

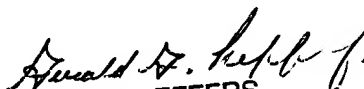
No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
AU 1636


GERRY LEFFERS
PRIMARY EXAMINER